Journal of Child Neurology
http://jcn.sagepub.com

Laparoscopic Nissen Fundoplication During Gastrostomy Tube Placement and Noninvasive Ventilation May Improve Survival in Type I and Severe Type II Spinal Muscular Atrophy

Nanci Yuan, Ching H. Wang, Anthony Trela and Craig T. Albanese

J Child Neurol 2007; 22; 727
DOI: 10.1177/0883073807304009

The online version of this article can be found at:
http://jcn.sagepub.com/cgi/content/abstract/22/6/727

Published by:
SAGE Publications
http://www.sagepublications.com

Additional services and information for *Journal of Child Neurology* can be found at:

Email Alerts: http://jcn.sagepub.com/cgi/alerts

Subscriptions: http://jcn.sagepub.com/subscriptions

Reprints: http://www.sagepub.com/journalsReprints.nav

Permissions: http://www.sagepub.com/journalsPermissions.nav

Citations (this article cites 12 articles hosted on the SAGE Journals Online and HighWire Press platforms):
http://jcn.sagepub.com/cgi/content/refs/22/6/727

Downloaded from http://jcn.sagepub.com at Stanford University on August 16, 2007
© 2007 SAGE Publications. All rights reserved. Not for commercial use or unauthorized distribution.

Original Article

Journal of Child Neurology
Volume 22 Number 6
June 2007 727-731
© 2007 Sage Publications
10.1177/0883073807304009
http://jcn.sagepub.com
hosted at
http://online.sagepub.com

Laparoscopic Nissen Fundoplication During Gastrostomy Tube Placement and Noninvasive Ventilation May Improve Survival in Type I and Severe Type II Spinal Muscular Atrophy

Nanci Yuan, MD, Ching H. Wang, MD, PhD, Anthony Trela, BS, and Craig T. Albanese, MD

Progressive respiratory muscle weakness with bulbar involvement is the main cause of morbidity and mortality in type I and severe type II spinal muscular atrophy. Noninvasive positive pressure ventilation techniques coupled with laparoscopic gastrointestinal procedures may allow for improved morbidity and mortality. The authors present a series of 7 spinal muscular atrophy patients (6 type I and 1 severe type II) who successfully underwent laparoscopic gastrostomy tube insertion coupled with Nissen fundoplication and early postoperative extubation using noninvasive positive pressure ventilation techniques. The authors measured the length of survival and the frequencies of pneumonia and hospitalization before and after surgery as outcomes of these new surgical and medical interventions. All 7 patients had respiratory symptoms (unmanageable oropharyngeal secretions, cough, pneumonia), difficulty feeding, and weight loss. Six patients had documented reflux via diagnostic testing preoperatively. Five patients were on noninvasive positive pressure ventilation and other supportive respiratory therapies prior to surgery. All 7 patients survived the procedures. By August 2006, 5 patients with type I and 1 with severe type II spinal muscular atrophy were alive and medically stable at home 1.5 months to 41 months post-op. One patient with type I expired approximately 5 months post-op due to obstructive apnea. This case series demonstrates that laparoscopic gastrostomy tube placement coupled with Nissen fundoplication and noninvasive positive pressure ventilation can be successfully used as a treatment option to allow for early postoperative extubation and to optimize quality of life in type I and severe type II spinal muscular atrophy patients.

Keywords: spinal muscular atrophy; laparoscopic Nissen fundoplication; gastrostomy tube; noninvasive positive pressure ventilation

Spinal muscular atrophy is the most common fatal neuromuscular disease of infancy with an incidence of 4.1 to 13.8 per 100 000 live births with a carrier frequency of approximately 1:50.[1] Spinal muscular atrophy is an autosomal recessive disorder that causes degeneration of motor neurons in the spinal cord and cranial nerve nuclei, resulting in profound weakness and hypotonia. Spinal muscular atrophy is classified based on 3 main factors: age at onset of symptoms, age of death, and the highest motor milestone achieved (eg, sitting or walking without support).[2] Type I patients (the most severe clinical form) present within the first few months of life with progressive weakness and usually suffer from malnutrition and respiratory insufficiency leading to aspiration and death before 2 years of age.[3,4] Patients with type II spinal muscle atrophy usually present at 6 to 18 months of life with progressive weakness and, in moderate to severe cases, also result in malnutrition and respiratory insufficiency.[3,4] There is a lack of published medical literature to date on the respiratory, nutritional, and surgical management of these patients. Until recently, previous published literature has been largely negative and resulted in less aggressive intervention in this population.[3,5]

There is growing literature showing that advances in pediatric noninvasive ventilation[6-9] and laparoscopic surgical antireflux procedures[10,11] may improve the quality of life in

From the Divisions of Pediatric Pulmonology (NY), Pediatric Neurology (CHW, AT), and Pediatric Surgery (CTA), Lucile Packard Children's Hospital, Stanford University Medical Center, Stanford, California.

Address correspondence to: Nanci Yuan, MD, Division of Pediatric Pulmonology, Lucile Salter Packard Children's Hospital, 701 Welch Road, Ste 3328-A, Palo Alto, CA 94304-5786; e-mail: nyuan@stanford.edu.

Yuan N, Wang CH, Trela A, Albanese CT. Laparoscopic Nissen fundoplication during gastrostomy tube placement and noninvasive ventilation may improve quality of life in type I and severe type II spinal muscular atrophy. *J Child Neurol*. 2007;22:727-731.

Downloaded from http://jcn.sagepub.com at Stanford University on August 16, 2007
© 2007 SAGE Publications. All rights reserved. Not for commercial use or unauthorized distribution.

children with various chronic medical illnesses. However, there are little published data on the outcomes of these therapeutic advances in the type I and type II spinal muscular atrophy populations. The purpose of this article is to describe our experience with 5 type I patients and 1 severe type II patient who successfully underwent laparoscopic Nissen fundoplication, gastrostomy tube placement, and noninvasive positive pressure ventilation at the Lucile Packard Children's Hospital at Stanford.

Methods

We performed a retrospective chart review of all patients with diagnosis of type I and type II spinal muscular atrophy who had been treated at the Lucile Packard Children's Hospital from January 2003 to July 2006. Initial diagnosis of spinal muscular atrophy was by clinical symptoms. All cases of type I spinal muscular atrophy were confirmed by homozygous deletion of the survival motor neuron (SMN1) gene. The diagnosis of the 1 patient with type II spinal muscular atrophy was confirmed by muscle biopsy and electromyography. Symptoms leading to the requirement for parenteral feeding were recorded. Surgical procedures and methods of postoperative care, including respiratory management of these patients, were documented. The length of survival and frequencies of pneumonia and hospitalization were measured as outcomes of these surgical and medical interventions.

Procedure of Laparoscopic Nissen Fundoplication During Gastrostomy Tube Placement

No paralytic agents were used during the procedure. The standard 4 or 5 trocar method for fundoplication was used. No procedure was converted to an open technique. Bupivicaine was instilled in all of the 3- to 5-mm trocar wounds at the end of the procedure. Rectal Tylenol was administered while the patients were anesthetized.

Procedure of Noninvasive Positive Pressure Ventilation

Noninvasive positive pressure ventilation was delivered with a BiPAP Vision bilevel airway pressure device (Respironics, Murrysville, Pa) using the Respironics petitesize infant mask. All patients also received aggressive pulmonary clearance interventions, including the CoughAssist In-Exsufflator (Emerson, Cambridge, Mass), aerosolized pulmonary medications, and chest physiotherapy. Noninvasive positive pressure ventilation settings (inspiratory and expiratory pressure, rise time, rate, and supplemental oxygen flow) were titrated to provide optimal patient synchrony and optimal oxygenation-ventilation as accessed by serum blood gas analysis, transcutaneous capnography (Respironics), and/or oxyhemoglobin saturation by pulse oximetry (Philips Agilent, Eindhoven, the Netherlands or Nellcor, Pleasanton, Calif).

Table 1. Patient Demographics and Diagnosis of Spinal Muscular Atrophy

Case	Gender	Ethnicity	Type of Spinal Muscular Atrophy	Age at Diagnosis, Months
1	Male	Caucasian	I	8
2	Female	Caucasian	I	3
3	Female	Asian	I	5
4	Female	Asian	I	4
5	Male	Asian	II	36
6	Female	Hispanic	I	1.5
7	Male	Caucasian	I	7

Results

Seven patients (6 type I and 1 severe type II) underwent laparoscopic Nissen fundoplication and gastrostomy tube placement at the Lucile Packard Children's Hospital between January 2003 and July 2006. There were 4 females and 3 males. Median age of diagnosis for type I spinal muscle atrophy patients was 4 months. The type II patient was diagnosed at 36 months. Three patients were Caucasian, 3 were Asian, and 1 was Hispanic (Table 1).

All patients pre- and post-op were followed by pediatric pulmonary medicine, neurology, and surgery. In all but 1 case, gastroenterology was involved. All 7 patients had respiratory symptoms (unmanageable oropharyngeal secretions, cough, pneumonia), difficulty feeding, and weight loss prior to being evaluated for gastroesophageal reflux. All patients had a multidisciplinary care conference to discuss multiple medical issues (resuscitation status, aspiration and reflux risks, medical vs surgical management). Six patients had documented reflux via diagnostic testing. Antireflux medication was administered as the initial course of treatment in all confirmed cases. Five patients were on noninvasive positive pressure ventilation prior to surgery. All patients were already receiving therapy via the cough-assist machine, pulmonary aerosol medications, chest physiotherapy, and suctioning prior to surgery.

All patients immediately post-op were followed in our pediatric intensive care unit and transferred to the general pediatric floor before being discharged home. All 7 patients survived Nissen fundoplication and gastrostomy tube placement. Of these 7 patients, 6 required noninvasive positive pressure ventilation immediately post-op, and 1 patient was extubated to room air. Average post-op pediatric intensive care unit stay was 3.6 days (range, 1-9 days), which was quite remarkable for post-op care for type I and severe type II spinal muscle atrophy patients (Table 2).

Downloaded from http://jcn.sagepub.com at Stanford University on August 16, 2007
© 2007 SAGE Publications. All rights reserved. Not for commercial use or unauthorized distribution.

Table 2. Patient Demographics: Surgery and Postoperative Results

Case	Age at Surgery, Months	Extubation Time, h	Extubation Type	PICU Stay, Days	Feeds Started, POD	Discharge, POD
1	46	1.5	Room air	1	1	3
2	8	1.0	NPPV	3	1	46
3	6	24	NPPV	2	1	2
4	5	1.0	NPPV	9	1	21
5	69	0.5	NPPV	1	1	5
6	5	1.0	NPPV	7	1	14
7	11	0.5	NPPV	2	2	4

NOTE: PICU, pediatric intensive care unit; POD, post-op day; NPPV, noninvasive positive pressure ventilation.

Table 3. Patient Demographics: Long-Term Survival

Case	Survival in Months Since Surgery	Current Survival Age, Months
1	41	87
2	22	30
3	19	25
4	5[a]	Expired
5	4	73
6	4	9
7	1.5	14

a. Expired.

By August 31, 2006, 5 patients with type I and 1 with severe type II spinal muscle atrophy were alive and medically stable at home 1.5 months to 41 months post-op (age range, 9-87 months). One patient with type I unexpectedly expired approximately 5 months post-op due to a non surgical-related event (she had an obstructive apnea episode when her airways became occluded during transport to a medical appointment) (Table 3).

We calculated the total number of inpatient and outpatient pneumonias before and after surgery. Pneumonias were diagnosed based on clinical history, physical examination, and chest radiograph. All pneumonias were treated with antibiotics. Patients were diagnosed either at our institution or at their local medical facility. We reviewed our medical documentation and confirmed results with the patient's family. One-month postsurgery data are available for all 7 patients. One month before surgery, 6 patients had a total of 8 pneumonias. One month after surgery, only 1 patient had 1 pneumonia. Three-month postsurgery data are available for 6 patients. Three months before surgery, 5 patients had a total of 5 pneumonias. Three months after surgery, only 2 patients had a total of 2 pneumonias. One patient has a 1-year set of presurgery and postsurgery data. This patient has had no pneumonias since his surgery (Table 4).

We calculated the total number of hospitalizations before and after surgery. Hospitalizations were defined as hospital room stays greater than 24 hours in duration. Patients were hospitalized at our institution or at their local medical facility. We reviewed our medical documentation and confirmed results with the patient's family. Hospitalizations were for pneumonia or mucus-plugging–induced respiratory distress. One-month postsurgery data are available for all 7 patients. One month before surgery, 6 patients had a total of 8 hospitalizations. One month after surgery, 2 patients had a total of 2 hospitalizations. Three-month postsurgery data are available for 6 patients. Three months before surgery, 5 patients had a total of 5 hospitalizations. Three months after surgery, only 2 patients had a total of 2 hospitalizations. One patient has a 1-year set of presurgery and postsurgery data. This patient has had no hospitalizations since his surgery (Table 5).

Discussion

We present a descriptive case series on our multidisciplinary experience with laparoscopic Nissen fundoplication during gastrostomy tube placement, as well as the early postoperative use of noninvasive positive pressure ventilation in the type I and severe type II spinal muscular atrophy population.

Although our case series is small in number, it is the largest in the published medical literature. The only other case series published dealing with the treatment of type I spinal muscular atrophy with noninvasive positive pressure ventilation and gastrostomy tube feeding was by Birnkrant et al in 1997.[4] In that case descriptive series, a total of 4 patients with type I spinal muscular atrophy were reviewed. Three patients had a gastrostomy tube, and 1 had a gastrojejunostomy tube placed. No patient underwent a Nissen fundoplication. In all 4 cases, survival was only 1 to 3.5 months after presenting with severe aspiration. All 4 patients developed worsening respiratory distress, and the families elected to keep the child at home to die. The constellation of aspiration, reflux, poor nutritional status, and respiratory complications seen in these patients demonstrates the multiorgan system disease of type I spinal muscular atrophy. It also points out the ethical dilemma in managing these patients.

Previous negative outcomes both in published medical literature and in anecdotal observations have resulted in a medical culture toward nonaggressive treatment in these patients. The article by Birnkrant et al[4] does not specifically state how the gastrostomy tubes were placed. But considering the year of publication, it is highly probable that these patients underwent open surgery versus a laparoscopic approach. It has been our experience at Lucile Packard Children's Hospital that peri- and post-op complications, including nutritional and pulmonary problems and pain, have been markedly reduced when this surgery is performed laparoscopically in the skilled hands of a pediatric surgeon.

Downloaded from http://jcn.sagepub.com at Stanford University on August 16, 2007
© 2007 SAGE Publications. All rights reserved. Not for commercial use or unauthorized distribution.

Table 4. Pneumonias in the Months Presurgery and Postsurgery

Case	Presurgery 12 Months	Presurgery 3 Months	Presurgery 1 Month	Presurgery Total	Postsurgery 1 Month	Postsurgery 3 Months	Postsurgery 12 Months	Postsurgery Total	Pre-Post[a]
1	2	1	0	3	0	0	0	0	–3
2	NA[b]	1	1	2	0	0	1	1	–2
3[c]	NA[b]	0	1	1	1	1	0	2	+1
4[d]	NA[b]	0	1	1	0	0	Expired	0	–1
5	2	1	2	5	0	0	NA[e]	0	–3
6	NA[b]	1	2	3	0	1	NA[e]	1	–2
7	NA[b]	1	1	2	0	NA[e]	NA[e]	0	–1

a. The difference is calculated during the time available for presurgery and postsurgery comparison.
b. Nonapplicable as patient was less than 12 months of age at time of surgery.
c. This patient has had no pneumonias since 3 months postsurgery.
d. This patient expired from an obstructive apnea at 5 months after surgery.
e. Nonapplicable as patient has not yet reached this postsurgery milestone.

Table 5. Hospitalizations in the Months Presurgery and Postsurgery

Case	Presurgery 12 Months	Presurgery 3 Months	Presurgery 1 Month	Presurgery Total	Postsurgery 1 Month	Postsurgery 3 Months	Postsurgery 12 Months	Postsurgery Total	Pre-Post[a]
1	2	1	0	3	0	0	0	0	–3
2	NA[b]	1	1	2	0	0	1	1	–2
3[c]	NA[b]	0	1	1	1	1	0	2	+1
4[d]	NA[b]	0	2	2	0	0	Expired	0	–2
5	2	1	1	4	0	0	NA[e]	0	–2
6	NA[b]	1	2	3	1	1	NA[e]	2	–1
7	NA[b]	1	1	2	0	NA[e]	NA[e]	0	–1

a. The difference is calculated during the time available for pre- and postsurgery comparison.
b. Nonapplicable as patient was less than 12 months of age at time of surgery.
c. This patient has had no hospitalizations since 3 months postsurgery.
d. This patient expired from an obstructive apnea at 5 months after surgery.
e. Nonapplicable as patient has not yet reached this postsurgery milestone.

Pain abatement is a known benefit of laparoscopic surgery.[10,11] Conventional Nissen fundoplication and/or gastrostomy tube placement requires a large, transverse upper (subcostal) abdominal incision. This painful incision results in diaphragmatic splinting and the need for opioids for pain control. Pain after the laparoscopic procedure is controlled with either Tylenol or Toradol, coupled with intraoperative infiltration of the 3- and 5-mm trocar sites with 0.25% Bupivicaine, which lasts 8 to 12 hours. No muscles are cut so the dynamics of breathing are minimally altered. Thus, we have been able to extubate our patients to noninvasive positive pressure ventilation or room air within 24 hours post-op. And our patients were able to be discharged home as early as 2 days post-op.

It is not our goal to push aggressive medical or surgical treatment in every child with type I or severe type II spinal muscular atrophy. However, due to the common and potentially fatal complication of aspiration and reflux, it is our policy that feeding methods and respiratory complications need to be addressed at diagnosis. We believe in a systematic but patient/family-centered approach to therapy. At diagnosis, we discuss all methods of feeding (oral, nasogastric, nasojejunal feeds, gastrostomy tube or gastrojejunostomy alone vs Nissen fundoplication and gastrostomy tube), including risks and benefits in an unbiased and sensitive approach. To help our patients/families in their decision, when warranted, we routinely send for further testing, including occupational therapist–modified barium swallow, pH probe, sleep apnea study, and an upper gastrointestinal series. We emphasize, however, that patients' clinical history and physical condition as well as natural history of the disease are more reliable than any tests performed. In our case series, many patients had initial and repeat testing that was negative for either reflux or aspiration, despite persistent episodes of pneumonia and respiratory distress. Prior to surgery, all 7 patients had respiratory symptoms (unmanageable oropharyngeal secretions, cough, pneumonia), difficulty feeding, and weight loss.

There was an average number of 1 pneumonia and 1 hospitalization per patient 1 month prior to surgery. One month after laparoscopic Nissen fundoplication performed during gastrostomy tube placement, the episodes of pneumonia and hospitalization were reduced to 1. Our 3-month postsurgery data are limited to 6 patients. However, the average numbers of pneumonias and hospitalizations per patient were both

Downloaded from http://jcn.sagepub.com at Stanford University on August 16, 2007
© 2007 SAGE Publications. All rights reserved. Not for commercial use or unauthorized distribution.

reduced by 50%. We acknowledge the lack of 12-month postsurgical data in our case series. However, our 1 patient who meets these criteria went from a total of 3 pneumonias requiring hospitalization prior to surgery to no pneumonias and no hospitalizations since surgery. We believe that in children with type I and severe type II spinal muscular atrophy, laparoscopic Nissen fundoplication should be performed regardless of whether reflux can be documented.

We believe that significant advances have been made in the pulmonary,[6-9] surgical,[10,11] and coordinated multidisciplinary care in the pediatric neuromuscular population.[12,13] Our interventions are not curative. However, we believe that our integrated approach has resulted in improved medical outcomes and quality of life, and it may improve length of survival in children with type I and severe type II spinal muscular atrophy when compared with published data and natural history studies.[1-3]

Acknowledgment

All work was done at Lucile Packard Children's Hospital, Stanford, California. This work was not supported by a grant or other form of funding. This material has not been presented at any meeting. There are no potential conflicts of interest or commercial support by any of the authors.

References

1. Zaldivar T, Montejo Y, Acevedo AM, et al. Evidence of reduced frequency of spinal muscular atrophy type 1 in the Cuban population. *Neurology*. 2005;65:636-638.
2. Hausmanowa-Petrusewicz I, Vrbova G. Spinal muscular atrophy: a delayed development hypothesis. *Neuroreport*. 2005;16:657-661.
3. Hirtz D, Iannaccone S, Heemskerk J, et al. Challenges and opportunities in clinical trials for spinal muscular atrophy. *Neurology*. 2005;65:1352-1357.
4. Birnkrant DJ, Pope JF, Martin JE, et al. Treatment of type 1 spinal muscular atrophy with non-invasive ventilation and gastrostomy feeding. *Pediatr Neurol*. 1998;18:407-410.
5. Hardart MK, Burns JP, Truog RD. Respiratory support in spinal muscular atrophy type I: a survey of physician practices and attitudes. *Pediatrics*. 2002;110(pt 1):e24.
6. Simonds AK, Muntoni F, Heather S, et al. Impact of nasal ventilation on survival in hypercapnic Duchenne muscular dystrophy. *Thorax*. 1998;53:949-952.
7. Wallis C. Non-invasive home ventilation. *Paediatr Respir Rev*. 2000;1:165-171.
8. Bach JR, Niranjan V, Weaver B. Spinal muscular atrophy type 1: a non-invasive respiratory management approach. *Chest*. 2000;117:110-115.
9. Bush A, Fraser J, Jardine E, et al. Respiratory management of the infant with type 1 spinal muscular atrophy. *Arch Dis Child*. 2005;90:709-711.
10. Sydorak RM, Albanese CT. Laparoscopic antireflux procedures in children: evaluating the evidence. *Semin Laparosc Surg*. 2002;9:133-138.
11. Rothenberg SS. Laparoscopic Nissen procedure in children. *Semin Laparosc Surg*. 2002;9:146-152.
12. Wallgren-Pettersson C, Laing NG. 109th ENMC International Workshop: 5th workshop on nemaline myopathy, 11th-13th October 2002, Naarden, The Netherlands. *Neuromuscul Disord*. 2003;13:501-507.
13. Finder JD, Birnkrant D, Carl J, et al. Respiratory care of the patient with Duchenne muscular dystrophy: ATS consensus statement. *Am J Resp Crit Care*. 2004;170:456-465.

Downloaded from http://jcn.sagepub.com at Stanford University on August 16, 2007
© 2007 SAGE Publications. All rights reserved. Not for commercial use or unauthorized distribution.